REMARKS

Claims 1-3 and 22 are pending in the present application. Claims 1-3 and 22 are rejected. Claims 4-21, and 23-24 have previously been cancelled.

By way of the present Amendment, claims 1 and 22 are amended and claim 2 is cancelled, herein.

Amendments to the Claims

Claim 1 has been amended to recite an isolated peptide consisting of SEQ ID NO.: 1 and defined variants thereof. Support for these amendments is found in the specification on page 12, lines 16-18, page 12, lines 23-24, page 12, lines 25-32, and in the chart on page 13, lines 1-11 above text.

Claim 22 has been amended to recite the identity of the peptide and to be rewritten in independent form.

No new matter is added by way of these amendments.

Rejections Under 35 U.S.C. § 101

Claims 1-2 stand rejected under 35 U.S.C. § 101 as being directed to non-statutory matter. To the extent that this rejection applies to claim 2, this rejection is rendered moot in view of the cancellation of this claim herein. Applicants' response to this rejection therefore applies solely to claim 1. Applicants have amended claim 1 to recite "an isolated neuron survival-promoting peptide..." Applicants respectfully submit that the rejection of claims 1-2 has been overcome and request that the rejection under 35 U.S.C. § 101 be withdrawn.

Rejections Under 35 U.S.C. § 112, first paragraph

Claims 1-3 and 22 stand rejected under 25 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time of filing. To the extent that this rejection applies to claim 2, this rejection is rendered moot in view of the cancellation of this claim herein. Applicants' response to this rejection therefore applies solely to claim 1, 3, and 22. Specifically, the Examiner is of the

opinion that a comparison of SEQ ID NOS. 1 and 2 does not reveal any critical amino acids that would characterize the genus of polypeptides encompassed by claim 1.

Applicants respectfully submit that the specification provides adequate written description for the claims as amended. Applicants remind the Examiner that:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see i)(A), above), reduction to drawings (see i)(B), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406. *See* MPEP § 2163. (emphasis added).

The specification characterizes CHEC-9 (SEQ ID NO.: 1) as a nine amino acid peptide that possesses demonstrable phospholipase A2 inhibitory activity, dramatically promotes neuronal survival, and suppresses the immune response to cortical lesions, in particular macrophage and microglia invasion at the site of injury (page 11-12). The specification further recites those amino acid substitutions that preserve this bioactivity. Further, inspection of an alignment of SEQ ID NOS.: 1 and 2 reveal that there is homology between the two peptides, in contrast to the Examiner's characterization of the peptides as "different." Residues 1, 4, 6, and 9 are identical. Residues 2, 3, 5, and 8 are all conservative amino acid substitutions as defined in the specification. Thus, rather than being "an invitation for discovery," the present specification provides a useful roadmap for the skilled artisan to identify variants of the peptides likely to retain the essential bioactivity described in the specification. Reconsideration and withdrawal of the rejection of claims 1, 3 and 22 under 35 U.S.C. § 112, first paragraph, for alleged lack of written description is respectfully requested.

Claims 1-3 and 22 stand rejected under 35 U.S.C. § 112, first paragraph, for lacking enablement. To the extent that this rejection applies to claim 2, this rejection is rendered moot in view of the cancellation of this claim herein. Applicants' response to this rejection therefore applies solely to claim 1, 3, and 22. The Examiner allows that the specification is enabled for an isolated peptide consisting of SEQ ID NO.: 1 or for kits comprising such a peptide. However, the Examiner is of the opinion that the specification is not enabled for a "CHEC-9 peptide, or variants thereof." It is the Examiner's view that the phrase "variant

thereof," as defined on pages 12-13 and 17-19 of the specification encompasses "random insertions, deletions, or substitutions of amino acids" (page 5, lines 9-10 of the pending Office Action; emphasis added). Applicants respectfully disagree.

At no point in the specification is the term "variants" defined to include "random insertions, deletions, or substitutions of amino acids." Indeed, the specification defines "variants" as peptides "wherein as few as 1 or as many as 9 amino acids are changed, provided that the peptide still promotes neuron survival, inhibits a brain's immune response to degenerating elements, and/or inhibits phospholipase A2" (page 12, lines 17-21; emphasis added).

The specification further characterizes variants as "preferably...conservative amino acid substitutions." A "conservative amino acid substitution" is defined as replacement of an amino acid with a functionally and biochemically equivalent amino acid" (page 12, lines 21-24 of specification).

Arguments presented above with respect to the written description are incorporated herein. Further, the test of enablement is not whether *any* experimentation is necessary, but whether, if experimentation is necessary, it is undue. MPEP §2164.01 (citing *In re Angstadt*, 537 F.2d 498, 504 (C.C.P.A. 1976)). The test is not merely quantitative, since a considerable amount of experimentation is permissible if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. See, In re Wands (CAFC) 8 USPQ2d 1400, at 1404. The fact that experimentation may be complex does not necessarily make it undue if the art typically engages in such experimentation. *Id.* Further, the specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public. MPEP §2164.05(a) (citing *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991).

At the time of filing of the present application, the ability to generating amino acid substitutions, especially in a small, 9-amino acid peptide, and screening peptides for a particular bioactivity, such as inhibition of phospholipase A2, was indisputably well-established in the art.

Thus, for the instant claims, both prongs of reasonableness of required experimentation are satisfied, (1) the required experimentation is routine in the art, and (2) the specification provides the guidance with respect to the "direction in which the experimentation should proceed."

Accordingly, Applicants respectfully submit that all of the Examiner's written description rejections have either been overcome, and therefore, Applicants request reconsideration and withdrawal of the rejections.

With respect to the name "CHEC-9 peptide" as recited in claim 22 lacking enablement, in an attempt to expedite the prosecution of the present application, the Applicant has amended claim 22 to recite "an isolated peptide consisting of the sequence of CHEASAAQC (SEQ ID NO.: 1), or a variant thereof, said variant comprising between 1-9 conservative amino acid substitutions and including SEQ ID NO.: 2."

The Examiner further rejects claim 22 on the grounds that the specification only discloses increased survival of SY5Y neuroblastoma cells and decreased macrophage/microglia proliferation after cortical lesion, but that the specification does not disclose a population, or populations of neurons that express CHEC-9 receptors (Pending Office Action, page 6, line 11 to 12), and that no guidance is provided for treating neurodegenerative diseases.

CHEC-9 is a 9 amino acid peptide that inhibits secreted phospholipase A2 (sPLA2) enzymes, including sPLAS2 activity found in plasma of rats and humans. As such, no receptors are required for its effectiveness as an enzyme inhibitor. While sPLA2 enzymes have long been targeted for anti-inflammatory therapies, inhibitors have had little clinical success (Springer et al., 2001, Curr. Pharm. Des.7:181-198; Abraham et al., 2003, Crit. Care Med. 31:718-728; Bradley et al., 2005, J. Rheumatol. 32:417-423). Most of these inhibitors have been designed to block the enzyme from binding its substrate, i.e. they are competitive inhibitors. This results in increased levels of unmodified substrate that compete successfully with the inhibitor, eventually overcoming the inhibition (Westley et al., 1996, J. Biol. Chem. 271:5347-5352). CHEC-9 is a uncompetitive inhibitor that binds the enzyme-substrate complex and actually becomes more effective as substrate and enzyme concentrations increase (Cunningham et al., 2006, J. Neuroinflammation 3:25).

In response to the Examiner's allegation that the specification is not enabled for treating a neurodegenerative disease, the Applicants submit herewith a Declaration of Dr. Timothy Cunningham, a co-inventor of the present invention, under 37 C.F.R. § 1.132. This Declaration describes data that provide proof of concept that CHEC-9 is an effective therapeutic tool in reducing symptoms of several neurodegenerative disorders based on data obtained from accepted rodent models of multiple sclerosis (MS) and amyotrophic lateral sclerosis (ALS) (See Declaration at paragraphs 2 – 6 and accompanying Figures 1 – 6).

Accordingly, Applicants respectfully submit that all of the Examiner's enablement rejections have been overcome, and therefore, Applicants request reconsideration and withdrawal of the rejections.

Rejections Under 35 U.S.C. § 102(b)

Claims 1-3 and 22 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Cunningham et al., 2000, Experimental Neurol. 163:457-468 ("the Cunningham reference"). To the extent that this rejection applies to claim 2, this rejection is rendered moot in view of the cancellation of this claim herein. Applicants' response to this rejection therefore applies solely to claims 1, 3, and 22. It is the Examiner's view that the use of the term "variant thereof" in the present application encompasses the Y-P30 polypeptide disclosed in the reference. Further, it is the Examiner's view that the Cunningham reference itself reasonably constitutes instructions for using the kit of claim 22.

It is well-established law that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." MPEP §2131 (quoting *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). "The identical invention must be shown in as complete detail as is contained in the . . . claim." *Id.* (quoting *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989) (emphasis added). In order for this rejection to have merit, the Cunningham reference must describe each and every element of the claims in order to be an anticipating reference as set forth under 35 U.S.C. §102(b). However, the Cunningham reference does not identify the nine amino acid CHEC-9 peptide claimed in the present invention.

Accordingly, Applicants respectfully submit that the Examiner's rejection does not apply, and request reconsideration and withdrawal of the rejection.

Double Patenting

Claims 1-3 stand rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 6 and 7 of U.S. Patent No. 6,262,024. To the extent that this rejection applies to claim 2, this rejection is rendered moot in view of the cancellation of this claim herein. Applicants' response to this rejection therefore applies solely to claims 1 and 3. Claim 1 has been amended herein to recite an isolated peptide consisting of SEQ ID NO.: 1 and defined variants thereof. Claim 3 depends from claim 1. Applicants respectfully submit that the amendments to the claims set forth in the present Amendment overcome this double patenting rejection and request a reconsideration and withdrawal of the rejection.

Summary

Applicants respectfully submit that all of the Examiner's rejections and objections have either been overcome or rendered moot. No new matter has been added by way of the present Amendment.

Favorable examination and allowance of the claims is hereby requested.

Respectfully submitted,
TIMOTHY J. CUNNINGHAM, ET AL.

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(Date)

By: _____

Kathryn Doyle, Ph.D, J.D.
DRINKER, BIDDLE & REATH, LLP
One Logan Square
18th and Cherry Streets
Philadelphia, PA 19103-6996
Telephone: (215) 988-2902
Facsimile: (215) 988-2757
E-Mail: kathryn.doyle@dbr.com
Attorney for Applicants

KH/KD